Environmental Health Perspectives
Vol. 60, pp. 321-325, 1985

Health Status of Japanese and Taiwanese After Exposure to Contaminated Rice Oil

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Mass poisonings, called Yusho and Yu-Cheng, occurred in western Japan in 1968 and central Taiwan in 1979, respectively. These occurrences were separately caused by ingestion of rice oils contaminated with polychlorinated biphenyls (PCBs), polychlorinated dibenzofurans (PCDFs) and polychlorinated quaterphenyls. The total intakes of PCBs and PCDFs by the patients were calculated to be, on the average, 633 and 3.4 mg for Yusho, respectively, and 973 and 3.84 mg for Yu-Cheng, respectively, similar amounts of the causal agents being ingested in both instances. Increased eye discharge, pigmentation of nails, skin and mucous membrane, acneform eruptions and feeling of weakness were the most notable symptoms for both the poisonings. The PCB concentrations in the blood of patients were 1–30 ppb for Yusho and 3–1156 ppb for Yu-Cheng five years and one year after the outbreaks, respectively. For the Yusho patients, the clinical severity was closely related to the total amount of rice oil consumed and to the blood PCB concentration and the gas chromatographic pattern of blood PCBs.

Introduction

A mass poisoning incident, called Yusho, occurred in western Japan, mainly in Fukuoka and Nagasaki Prefecture, in 1968. Yusho was caused by ingestion of rice oil which was contaminated with Kanechlor 400, a commercial brand of Japanese polychlorinated biphenyls (PCBs) (*1,2*). It was found later that the rice oil was contaminated with not only PCBs but also polychlorinated dibenzofurans (PCDFs) and polychlorinated quaterphenyls (PCQs) (*3,4*). Consequently, Yusho was a poisoning by a mixture of PCBs, PCDFs and PCQs. The total number of Yusho patients identified was 1788 at the end of 1982. In 1979, eleven years after the Japanese Yusho incidence, a similar mass poisoning called "Yu-Cheng" occurred in central Taiwan; by the beginning of 1983 a total of 2060 patients had been identified. The cooking oil consumed by Yu-Cheng patients was also contaminated with PCBs, PCDFs and PCQs. This paper reviews the health status of the patients in Japan and Taiwan in relation to these causal agents.

Causal Agents

The epidemiological study on Yusho (*2*) indicated that the patients ingested rice oil produced and shipped by K company (abbreviated K rice oil) on February 5 and 6 1968 and several days thereafter. The patients with Yu-Cheng were found to have consumed cooking rice oil manufactured by C company (abbreviated C rice oil) (*5*). Some of the K and C rice oils were analyzed for PCBs, PCDFs and PCQs. Concentrations of these agents in the rice oils are summarized in Table 1. K rice oil contained these compounds at levels approximately 10 times higher than C rice oil (*6*). However, total intakes of PCBs, PCDFs and PCQs by Yusho and Yu-cheng patients were at similar levels, because total intakes of the oil were estimated on average to be 688 mL for Yusho patients and ca 12.3 kg for Yu-Cheng patients (*7,8*). Hayabuchi et al. (*7*) calculated the total intakes of PCBs and PCDFs by Yusho patients as 633 and 3.4 mg on average, respectively, while Lan et al. (*8*) estimated these values for Yu-Cheng patients as 973 and 3.84 mg, respectively. The similarity of these intakes

Table 1. Concentration of PCBs, PCDFs and PCQs in the rice oils from Fukuoka and Taiwan.[a]

	Concentration, ppm		
	K rice oil (Fukuoka)	C rice oil (Taiwan)	
		A	B
PCDFs	900	60	100
Unknown tetra-	0.65	0.04	0.05
2,3,7,8-Tetra-	0.20	Tr[b]	Tr[b]
2,3,4,7,8-Penta-	0.70	0.02	0.02
2,3,4,6,7-Penta-	0.35	0.01	0.02
1,2,3,4,7,8-Hexa-	0.12	0.01	0.01
1,2,3,6,7,8-Hexa-			
Total	2.02	0.08	0.10
PCQs	800[c]	90[c]	180[c]

[a]Data from Masuda et al. (*6*).
[b]Tr = 0.001–0.005 ppm.
[c]Approximate concentration.

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was partly caused by the difference in habitual usage of vegetable oil in Japanese and Chinese dishes.

Components of PCBs in K and C rice oils were somewhat different, as shown in Figure 1. C rice oil consisted more of the PCBs with comparatively higher boiling points than K rice oil. The major components of PCDFs in K and C rice oils were very similar, as shown in Table 1, though their concentrations were much higher in K rice oil.

Clinical Status

The symptoms of Yusho have slowly changed over 15 years after the outbreak. The dermal and mucosal signs, which were the most marked in the early stage, have gradually improved, while some general symptoms which are probably due to internal disturbance have become prominent in recent years. Initial symptoms experienced by 189 Yusho patients are summarized in Table 2. Eye discharge, pigmentation of nails, skin and mucous membrane, acneform eruption and feeling of weakness were the most notable symptoms (*2*).

Twenty-seven Yu-Cheng patients in three generations of a large family were examined for distinctive clinical features in 1979. The results are shown in Table 3. As with Yusho, hypersecretion of the Meibomian glands, pigmentation of nails, conjunctiva, gingiva, lips and face, and acneform eruption were observed (*9*). The

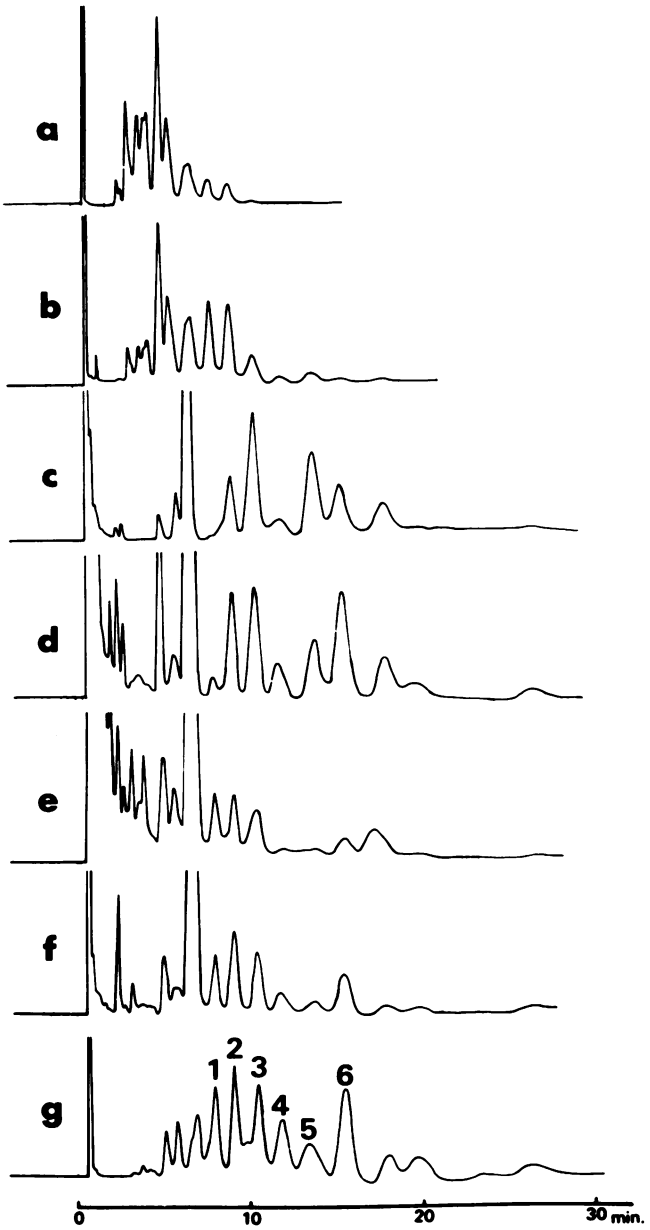

FIGURE 1. Gas chromatograms of PCBs on 2.5% SE-30 column: (*A*) Kanechlor 500; (*B*) Kanechlor 400 + Kanechlor 500 (1:1); (*C*) C rice oil (Taiwan); (*D*) K rice oil (Fukuoka).

Table 2. Distribution of symptoms of Yusho reported by 189 patients examined before October 31, 1968.[a]

Symptoms	% citing symptom	
	Males (N = 89)	Females (N = 100)
Dark brown pigmentation of nails	83.1	75.0
Distinctive hair follicles	64.0	56.0
Increased sweating at palms	50.6	55.0
Acnelike skin eruptions	87.6	82.0
Red plaques on limbs	20.2	16.0
Itching	42.7	52.0
Pigmentation of skin	75.3	72.0
Swelling of limbs	20.0	41.0
Stiffened soles in feet and palms of hands	24.7	29.0
Pigmentated mucous membrane	56.2	47.0
Increased eye discharge	88.8	83.0
Hyperemia of conjunctiva	70.8	71.0
Transient visual disturbance	56.2	55.0
Jaundice	11.2	11.0
Swelling of upper eyelids	71.9	74.0
Feeling of weakness	58.4	52.0
Numbness in limbs	32.6	39.0
Fever	16.9	19.0
Hearing difficulties	18.0	19.0
Spasm of limbs	7.9	8.0
Headache	30.3	39.0
Vomiting	23.6	28.0
Diarrhea	19.1	17.0

[a]Data from Kuratsune et al. (*2*).

Table 3. Distribution of symptoms and signs of 27 Yu-Cheng cases examined before December 15, 1979.[a]

Symptoms and signs	% reporting symptom or sign	
	Males (N = 15)	Females (N = 12)
Increased eye discharge	93.3	91.6
Swelling of eyelids	86.6	91.6
Acneform eruption	86.6	83.3
Pigmentation of nails	86.6	83.3
Pigmentation of conjunctivae	80	83.3
Pigmentation of lips	80	66.6
Black color of nose	66.6	75
Hyperemia of conjunctivae	66.6	75
Hypesthesia	60	58.3
Deformity of nails	53.3	66.6
Pigmentation of gingivae	53.3	50
Numbness of limbs	53.3	50
Amblyopia	46.6	66.6
Keratotic plaques of palms and soles	46.6	25
Distinctive hair follicles	40	41.6

[a]Data from Li et al. (*9*).

symptoms of Yusho and Yu-Cheng observed in the early stage were very similar.

Yusho can show chronic symptoms of the poisoning more than 10 years after the onset. Asahi et al. (*10*) reported that skin symptoms have diminished gradually during the ten years since the onset, while continual subcutaneous cyst formation with secondary infection was still occurring in a relatively small number of the severe grade patients. According to the report by Kohno and Yamana (*11*), several ocular signs have remarkably subsided during the past 10 years, but 84% of the 75 patients showed somewhat abnormal changes of the Meibomian glands, such as irregular arrangements, atrophy, secretion of cheeselike material, infarction and lithiasis, and 43% showed pigmentation of eyelids and conjunctiva. Eye discharge was still cited by 64% of the patients as a current complaint. Most Yusho patients complained of various neurological symptoms, such as hypoesthesia and neuralgia of the limbs (*12*). The following symptoms have also been mentioned by the majority of the patients, namely, general fatigue, poor appetite, inconstant abdominal pain, heavy headache, feeling of numbness and pain in the limbs, and cough and expectoration of sputum. Taiwanese Yu-Cheng patients will continue to exhibit symptoms for a long time unless proper treatments are applied.

Death among the Patients

Up to the end of 1982, 112 Yusho patients had died. Of these, 31 victims whose cause of death has been confirmed were classified as in Table 4 (*13*). There have been 11 deaths from neoplasms, 35.4% of the total. Among the Yu-Cheng patients 24 deaths were reported; half of them were from hepatoma, liver cirrhosis or liver diseases with hepatomegaly (*5*).

Table 4. Causes of death in Yusho patients (to 1977).[a]

Cause of death	Number of deaths
Malignant neoplasms	
Stomach cancer	2
Stomach cancer + liver cancer	1
Liver cancer + liver cirrhosis	2[b]
Lung cancer	2[b]
Lung tumor	1
Breast cancer	1
Malignant lymphoma	2
Total neoplasms	11
Cerebrovascular lesions	7
Traffic accidents	3
Pneumonia + pulmonary fibrosis	2
Myocardial degeneration + pericarditis	2[b]
Amyloidosis	1[b]
Osteodystrophia fibrosia	1[b]
Status thymicolymphaticus	1[b]
Liver cirrhosis	1
Suicide	1
Senility	1
Total	31

[a]Data from Urabe et al. (*13*).
[b]Autopsied cases.

PCBs, PCDFs and PCQs in the Patients

The concentration of PCBs in the liver and adipose tissue of six Yusho patients who died in 1969–1972 were 0.1 and 2.5 ppm, respectively on the average. The average PCB concentration in the blood of Yusho patients was 6.7 ppb ($N=41$) five years after the outbreak. These PCB concentrations were only two or three times higher than those of normal persons (*14*). The PCB level in the blood of 613 Yu-Cheng patients within the first year of outbreak (Table 5), ranged from 3 to 1156 ppb (*5*). The level in the patients was much higher than the PCB level in the blood of Taiwanese controls (mean ± SD; 1.2 ± 0.7 ppb, $N=29$) and the blood PCB level of Yusho patients described above. The difference in Yu-Cheng and Yusho patients is presumably due mainly to the time of sampling, that is, one year for Yu-Cheng and five years for Yusho after the respective outbreaks.

The gas chromatographic pattern of the majority of Yusho patients was different from that of normal persons, with a relatively lower peak 1 and a higher peak at 5 for Yusho as shown in Figure 2. Hence, gas chromatographic patterns of PCBs in the blood of Yusho patients were divided into three types, namely, (A) peculiar to Yusho; (B) resembling A; and (C) similar to the PCB gas chromatogram of normal persons (*15*).

The concentrations of PCDFs in the adipose tissue and liver of three Yusho patients who died in 1969–1972 were in the range 6–13 ppb and 3–25 ppb, respectively, while no PCDFs were detected at the detection limit of 0.05 ppb in the same tissues of persons who had been killed by traffic accidents (*16*). In the blood of Yusho and Yu-Cheng patients, PCDFs were also identified at the levels of 3 and 200–360 ppt, respectively, by Rappe et al. (*17*), and no detection (< 10 ppt) and 140 ± 70 ppt (mean ± SD, $N=15$), respectively, by Kashimoto et al. (*18*).

The blood of Yusho patients sampled in 1979 was analyzed for PCQs. The average concentrations were 2.9 ppb ($N=31$) for PCB gas chromatograms of type A, 2.0 ppb ($N=4$) for type B and 0.02 ppb ($N=29$) for type C (*19*). The PCQ concentrations are closely related to the PCB concentration and patterns in the blood. The blood PCQ level of Yusho patients was much lower than

Table 5. Blood PCB level in Yu-Cheng patients in Taiwan.[a]

PCB level, ppb	Number of patients	Percentage of patients
<10	29	4.73
11–50	143	23.73
51–100	272	44.37
101–150	91	14.84
151–200	28	4.57
201–300	24	3.92
301–400	17	2.77
401–500	4	0.65
>500	5	0.82
Total	613	100.00

[a]Data from Hsu et al. (*5*).

that of Yu-Cheng patients, which was determined as 19.3 ± 13.0 (mean ± SD, $N = 15$) by Kashimoto et al. (*18*).

Relationship between the Causal Agents and Clinical Symptoms

The mean latent period was estimated to be 71 days for Yusho and ca. 80 days for Yu-Cheng (*7,8*). The average amounts of PCBs, PCDFs and PCQs ingested by Yusho patients during the latent period were calculated to be 466, 2.5 and 439 mg, respectively, while Yu-Cheng patients consumed 302 mg of PCBs and 1.26 mg of PCDFs during the latent period (*7,8*). The smallest amounts ingested by a Yusho patient during the latent period were estimated to be 111 mg of PCBs, 0.6 mg of PCDFs and 105 mg of PCQs (*7*).

The PCB concentrations in the blood of Yusho patients five or more years after the poisoning showed a significant positive correlation with the total amount of rice oil consumed but not with the amount of the rice oil consumed per kg day (*7*). The clinical severity of the patients also showed a close positive correlation with the total amount of the oil consumed but not with the amount of the oil consumed per kg day (*20*). These observations can probably be explained as follows. The PCBs retained in the patients were only small portions of the PCBs in the rice oil, but they are very persistent in the patients as shown in Figure 2 and reflect the PCB concentrations in the blood and tissues of the patients several years after the outbreak. Consequently, the patients with higher blood PCB concentrations consumed a proportional amount of the rice oil which contained PCBs and very toxic PCDFs.

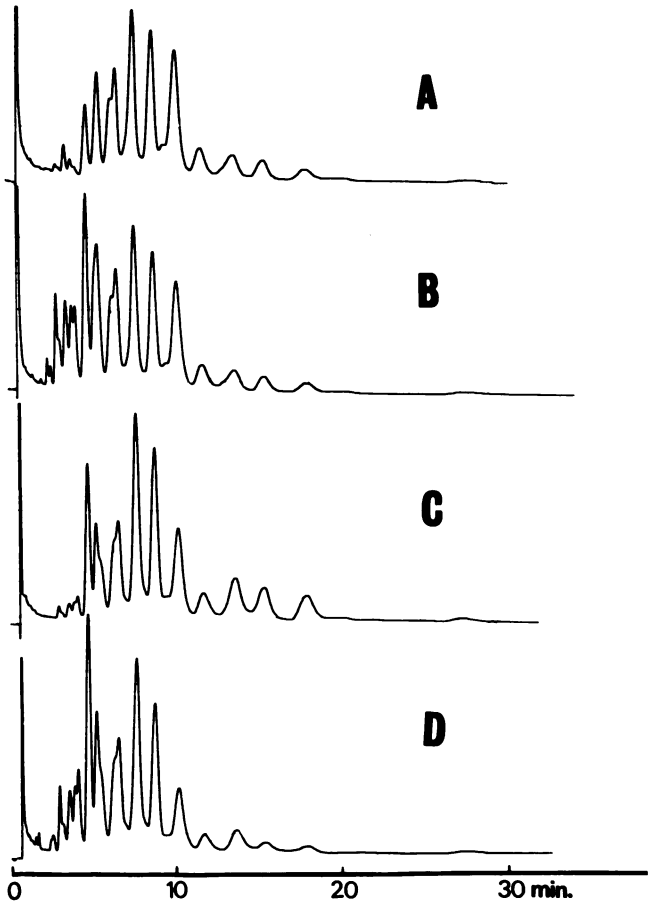

FIGURE 2. Gas Chromatograms of PCBs on 5% SE-30 column: (*a*) Kanechlor 400; (*b*) K rice oil; (*c,d*) blood of typical Yusho patients; (*e*) blood of Yusho patient; (*f*) blood of normal control; (*g*) Kanechlor 500 + Kanechlor 600 (1:1).

Gas chromatographic pattern, blood PCBs concentrations as well as clinical symptoms of 72 patients with Yusho were examined (Table 6). Dermatological symptoms were observed mostly in the type A group of blood PCBs. Type C group showed few such symptoms. General signs such as fatigue and headache were cited by patients with all types of PCB patterns (*21*).

The relationship between the PCB concentration or PCB pattern in the blood and ocular signs was examined in 238 persons, including 90 Yusho patients, in 1976 by Ohnishi and Yoshimura (*22*). The frequency of both abnormal pigmentation of the conjunctiva and hypersecretion of the Meibomian glands increased as the PCB concentration in the blood increased. Positive ocular signs also increased in frequency in the order of PCB pattern C < B < A.

Shigematsu et al. (*23*) examined 401 patients with Yusho for respiratory symptoms and PCB concentration and pattern in the blood. The respiratory symp-

Table 6. Gas chromatographic pattern of blood PCBs and incidence of clinical symptoms among Yusho patients (April 1973–March 9, 1974).[a]

Clinical symptoms	Incidence, no. of cases (%)			
	Type A (43 cases)	Type B (26 cases)	Type C (3 cases)	Total (72 cases)
Pigmentation				
Skin	22 (51)	0	0	22 (31)
Palpebra	31 (72)	5 (19)	0	36 (50)
Gingiva	41 (95)	15 (58)	2 (67)	58 (81)
Nail	32 (76)	9 (35)	0	41 (57)
Acneform eruption	15 (35)	0	0	15 (21)
Comedo	15 (35)	6 (23)	0	21 (29)
Infection of skin	14 (33)	3 (12)	0	17 (24)
Deformation of nails	28 (56)	10 (38)	0	38 (53)
Alopecia	0	1 (4)	0	1 (1)
Tooth disorders	8 (19)	2 (8)	0	10 (14)
Meibomian gland hypersecretion	40 (93)	21 (81)	3(100)	64 (89)
Fatigue	21 (49)	15 (58)	1 (33)	37 (51)
Fever	1 (2)	1 (4)	0	2 (3)
Phymata in articular region	4 (9)	2 (8)	0	6 (8)
Cough and sputum	28 (65)	12 (46)	1 (33)	41 (57)
Digestive disorder	15 (35)	12 (46)	2 (67)	29 (40)
Headache	20 (47)	9 (35)	1 (33)	30 (42)
Numbness of extremities	15 (52)	8 (31)	1 (33)	24 (33)
Menstrual disturbance	5/17 (29)	2/9 (22)		7/26 (27)
Concentration of blood PCBs (mean ± SD), ppb	7.2 ± 4.9	4.3 ± 3.1	1.7 ± 0.2	5.9 ± 4.8

[a]Data from Koda and Masuda (*21*).

toms were cough, expectoration and wheezing. The incidence of these symptoms correlated well with the concentration of PCBs in the blood but not with the pattern of PCBs.

Iwashita et al. (*24*) studied the frequency of headache and blood PCB concentration and pattern in 208 persons in a general examination for Yusho in 1973. Frequency of headache was 59.6–66.8%, but no relationship was observed between the headache frequency and the blood PCB concentration or pattern.

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